REMARKS

After entry of this amendment, claims 1-29 are pending. Claims 1, 5, 6, 13, 28 and 29 have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. Claim 1 finds further support in the specification at page 40, lines 30-31. No new matter has been added.

In response to the restriction requirement set forth in the Office Action mailed March 31, 2009, Applicants provisionally elect Group I, claims 2 (part a) and 10, drawn to a method for producing a transgenic plant that utilizes two expression cassettes within one DNA construct, wherein said method comprises a step of excising one of the expression cassettes, with traverse. Reconsideration and withdrawal of the restriction requirement is strongly urged in light of the present amendment and for the following reasons.

The Claimed Inventions Share a Special Technical Feature

Because this application is a national stage filing pursuant to 35 U.S.C. § 371, unity of invention under PCT Rule 13.1 and 13.2 is the applicable standard. Unity of invention is fulfilled "when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical feature. The expression 'special technical feature' shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." (PCT Rule 13.2).

The Examiner alleges that the inventions of Groups I-LXXVI do not relate to a single inventive concept because they lack the same or corresponding special technical feature under PCT Rule 13.2. In support, the Examiner states that the technical feature linking the groups is a DNA construct or method that utilizes a D-amino acid oxidase as a selection marker, and provides for excision of the selection marker or for segregation of the selection marker away from an expression cassette conferring an agronomically valuable trait, which is known in the art, citing Nasholm *et al.* (hereinafter "Nasholm") and Dale *et al.* (hereinafter "Dale"). Applicants respectfully disagree with the Examiner's characterization of the references and the inventions.

As stated in the specification and repeated in the claims, the general inventive concept of the present invention relates to improved construct and methods for eliminating marker

sequences from the genome of the plants using a dual-function selection marker which can act as both negative and counter-selection marker. See Specification at page 1, lines 6-9. Thus, contrary to the Examiner's characterization, the technical feature linking the groups is the use of a D-amino acid oxidase as a positive and negative selection marker in the same cells. For instance, the claimed method (*i.e.* claim 1 and the claims dependent therefrom) includes steps for positive and negative selection based on a single expression cassette comprising the D-amino acid oxidase gene. Both positive and negative selections are, therefore, based on the D-amino acid oxidase in the same cells. Similarly, the product claims (*i.e.* claim 11 and claims dependent therefrom) direct to a DNA construct that comprises a nucleic acid sequence encoding a D-amino acid oxidase. Thus, the D-amino acid oxidase gene contained in the claimed DNA construct can be used as a positive and negative selection marker when the DNA construct is transformed into the same cells.

The Examiner relies on Nasholm for teaching that D-amino acids may be used as selection markers when plants are transformed with a nucleic acid expressing a D-amino acid metabolizing protein such as a D-amino acid oxidase in addition to a polypeptide that may alter the phenotype of a plant in an advantageous manner. The Examiner further relies on Dale for teaching that selection genes can be excised from the transgenic plant's genome. The Examiner thus concludes that it would have been obvious to one skilled in the art to modify the methods taught in Nasholm to include a subsequent step of excising the selectable marker as taught by Dale. Applicants respectfully disagree.

Nasholm discloses a gene encoding an enzyme that metabolizes a D-amino acid and plants express such a gene in order to utilize D-amino acid as a nitrogen source and grow on media which would not otherwise support growth of the wild-type plant. See Nasholm, page 2, lines 24-28. As noted by the Examiner, Nasholm also teaches that D-amino acids may be used as selection markers by transforming a plant with a nucleic acid expressing a D-amino acid metabolizing protein. However, in order to maintain the transformed plant's ability to utilize D-amino acid as a nitrogen source and grow on media which would not otherwise support growth of the wild-type plant, one skilled in the art would not modify the method taught in Nasholm to include a subsequent step of excising the selection marker from the plant genome as taught by Dale as suggested by the Examiner.

Alternatively, the Examiner states that it would have been obvious to modify the method taught in Dale by replacing the hpt gene with one of the D-amino acid oxidase genes taught in Nasholm because this is a substitution of an equivalent element that was known in the art. Applicants respectfully disagree.

It is noted initially that the selection marker gene taught in Dale and the D-amino acid oxidase gene taught in Nasholm is fundamentally different. First, the selection marker gene taught in Dale, *i.e.* the hpt gene, can only be used for positive selection. The D-amino acid oxidase, on the other hand, as shown by the present application, can be used for positive and negative selection of the same transgenic cells or plants. Furthermore, as shown by the present application, the D-amino acid oxidase metabolizes two different compounds (compound X and compound M), while the selection marker encoded by the htp-gene metabolizes only one compound. Thus, although both genes can be used as selection markers, they are not equivalent substitutions as alleged by the Examiner.

Moreover, even if one skilled in the art would have substituted the selection marker used in the method taught in Dale with the D-amino acid oxidase gene taught in Nasholm, the method so modified would not render the present application obvious for the following reasons.

Dale discloses a method of gene transfer wherein the gene used as selection marker during the transformation is excised from the transgenic plant genome using the bacteriophage P1 Cre/*lox* recombination system. According to the method taught in Dale, the plants transformed with the selection marker, *i.e.* the hpt gene, require a second transformation step to introduce and express the Cre recombinase, which in turn deletes the htp gene from the plant genome. Because of the removal of the selection marker, the transgenic plants free of selectable marker could be selected only by random test of progeny plants.

Contrary to the method taught in Dale, the method taught in the present application allows for positive and negative selection of the same cells or plants. Thus, the cells or plants free of selectable marker need not be identified in a random collection of individuals. Rather, the cells or plants with the selection marker removed can be selected for, either directly via regeneration of transgenic cells or via selection of progeny plants during crossing away of the selection marker.

It follows that even if the D-amino acid oxidase gene taught in Nasholm is used to substitute the hpt gene in the method taught in Dale, the modified method would not have been the same as the method taught in the present application. Nor would the modified method render the method taught in the present application obviousness because the two methods are fundamentally different.

Because one skilled in the art would not have combined the cited references, and because, even if the references are combined, the combined teaching would not render the present application obvious, the Patent Office has not establish the presence of the special technical feature of Applicants' claims in the prior art. Accordingly, Applicants respectfully request that the Examiner reconsider the restriction requirement and examine all the claims in one application.

The International Examiner Found Unity of Invention

Furthermore, unity of invention was found during the international stage. As shown in the International Preliminary Report on Patentability and International Search Report, all claims were searched and examined together. Thus, application of PCT Rules 13.1 and 13.2 by the International Examiners shows that unity exists. Since the search has already been conducted by the International Search Authority and the International Examination Authority and no lack of unity of invention has been found, for this additional reason, there would be no undue burden on the Examiner to examine both Groups in one application.

CONCLUSION

For at least the above reasons, Applicants respectfully request that the restriction requirement be reconsidered and withdrawn.

In the event that the Examiner decides to maintain the original restriction requirement, Applicants provisionally elect Group I, claims 2 (part a) and 10 (with traverse), for further prosecution.

Applicants reserve all rights to pursue the non-elected species in one or more divisional applications.

Applicants are submitting their response within the one-month response period. No fee is believed due. However, if any fee is due, the Director is hereby authorized to charge our Deposit

Account No. 03-2775, under Order No. 13987-00022-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /s/ Hui-Ju Wu

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